UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/684,796	10/14/2003	Jonathan David Garman	020054-003610US	4233

20350 7590 09/16/2008

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
HOWARD, ZACHARY C	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
09/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/684,796	GARMAN ET AL.	
	Examiner	Art Unit	
	ZACHARY C. HOWARD	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *5-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *5-12* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 6/16/08 has been entered in full. Claim 1 is amended.

Claims 1-12 are pending.

Claims 5-12 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the 4/25/06 reply.

Claims 1-4 are under consideration.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (7/13/07).

The objection to the specification at pg 2 is *withdrawn* in view of Applicants' amendments to the specification.

The rejection of claims 1-4 under 35 U.S.C. § 112, first paragraph at pg 8-9 for failing to comply with the written description requirement is *withdrawn* in view of Applicants' amendments to the claims and on further consideration by the Examiner in view of the Written Description Training Materials Revision 1, 3/25/08 (http://www.uspto.gov/web/menu/written.pdf).

The rejection of claims 1 and 4 under 35 U.S.C. § 102(b) at pg 11-12 as being clearly anticipated by Schepens et al (1997) is *withdrawn* in view of Applicants' amendments to independent claim 1.

The rejection of claim 2 under 35 U.S.C. § 103(a) at pg 12-13 as being unpatentable Schepens et al (1997) as applied to claim 1, and further in view of Suzuki et al (1997) is *withdrawn* in view of Applicants' amendments to independent claim 1.

The rejection of claim 3 under 35 U.S.C. § 103(a) at pg 13 as being unpatentable Schepens et al (1997) as applied to claim 1, and further in view of Mathis et al (1957) is *withdrawn* in view of Applicants' amendments to independent claim 1.

Maintained Objections and/or Rejections

Claim Rejections - 35 USC § 101, utility

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. This rejection was set forth previously at pg 3-4 of the 7/13/07 Office Action.

Applicants' arguments (6/16/08; pg 6-8) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants divide the response to the rejection into two sections, (A) and (B). Each section and part will be addressed in turn.

In section (A), part (i), Applicants argue that the claimed methods can be used to identify modulators of binding between A2ARs and PDZs, and that this in itself provides utility to the claims. Applicants point to *Cross v. Iizuka* (1985) as commenting "on the significance of data from *in vitro* testing". In section (A), part (ii), Applicants argue that the "*in vitro* binding results of the claimed methods are indeed reasonably predictive of physiologically relevant interactions *in vivo*" (pg 7).

Applicants' arguments have been fully considered but are not found persuasive. The Examiner does not dispute the portion of *Cross v. Iizuka* quoted by Applicants; as stated therein, "*in vitro* testing may establish a practical utility". However, a key word used therein is "may". An invention with an asserted utility based on *in vitro* testing must still meet the requirements of 35 U.S.C. 101 by providing a specific and substantial utility. For the reasons set forth previously, the invention of claims 1-4 does not have a specific and substantial utility. In particular, the asserted utility (to determine the binding between alpha adrenergic receptors and PDZ proteins, such that the binding can be modulated for therapeutic purposes) is not a substantial utility. A substantial utility is a practical use which amounts to more than a starting point for further research and investigation and does not require or constitute carrying out further research to identify or reasonably confirm what the practical use might ultimately be. Basic research, such

as studying the properties of the claimed product or the mechanisms in which the product is involved, does not constitute a substantial utility.

In the instant case, the asserted utility is not a specific and substantial utility because there is no reasonable correlation between the ability of a particular PDZ protein to bind to an α2 adrenergic receptor and the ability to modulate the activity of said receptor by altering said binding. The specification in Tables 8A-C provides a long list of PDZ proteins that each have some degree of binding to a small fragment of an alpha-adrenergic receptor sequence in an *in vitro* binding assay. However, the ability to bind to a small fragment of a receptor sequence *in vitro* does not indicate whether or not modification of said binding will actually modify the activity of the receptor protein either *in vitro* or *in vivo*. Binding assays frequently identify protein-protein interactions that have no physiological significance. For example, the relevant art questions the physiological significance of binding between a C-terminal peptide of human α1A-adrenergic receptor and the PDZ domain of neuronal nitric oxide synthase (nNOS). Schepens et al (1997) demonstrated (using a yeast two-hybrid assay) that a protein consisting of the last 114 amino acids of the rat α1C (later renamed α1A) adrenergic receptor was able to bind to the PDZ domain of neuronal nitric oxide synthesis (nNOS; Schepens et al, 1997. FEBS Letters. 409: 53-56; cited previously). However, Pupo et al (2002) later conclude, "nNOS does interact with full-length α1A-ARs, but that this interaction is not subtype-specific and does not require the C-terminal tail, raising questions about its functional significance" (see Abstract of Pupo et al, 2002. BMC Pharmacology. 2: 17-23; cited on the 10/11/05 IDS). Importantly, Pupo teaches, "[s]tudies on α1A-ARs in transfected PC12 cells showed no role for nitric oxide in mitogenic signaling, also raising questions about the functional significance of this interaction" (pg 6).

Applicants further argue that this single example of an AAR-PDZ interaction (Schepens et al, 1997; cited previously) "for which the in vivo relevance was later questioned" (in Pupo et al, 2002) is "insufficient to demonstrate a lack of utility" (pg 7-8).

Applicants' arguments have been fully considered but are not found persuasive. It is maintained that the single example of an interaction described in *Schepens* et al

(1997) and *Pupo* et al (2002) is highly relevant to consideration of the utility of the claimed invention. The experiments described by Pupo et al provide evidence of the standard in the art in the art in order to recognize whether or not an observed binding interaction is biologically relevant. Applicants' experiments do not meet this standard; Applicants merely describe a cell-free *in vitro* binding reaction without providing any evidence of physiological relevance. Applicants' experiments describe a binding reaction between a small portion (20 amino acids) of the C-terminus of three related receptor proteins and a number of PDZ proteins. Significantly, this experiment is conducted *in vitro* in highly artificial conditions that are not representative of *in vivo* intracellular conditions. The specification states, "The background binding is somewhat high for these peptides (average OD), and a reduced number of interactions would be seen with lower peptide concentrations", which would lead the skilled artisan to question whether any of these interactions actually occur *in vivo*. It is also not clear whether or not a negative control was even used. Furthermore, the recited sequences of SEQ ID NO: 26 (comprising "RIV"), 27 (comprising "TAW") and 28 (comprising "FRQ") do not match any of the known consensus PDZ-binding sequences known in the art at the effective filing date of the instant application. See Bezprozvanny et al, 2001 (FEBS. 509: 457-462), who teaches that type I PDZ domains are specific for the consensus sequence S/T-X-Φ (where Φ is a hydrophobic amino acid); type II PDZ domains are specific for the consensus sequence Φ-X-Φ; that the PDZ protein nNOS is specific for the sequence G-E/D-X-V; and that the PDZ protein Mint1-1 is specific for the sequence E/D-X-W-C/S (pg 457). Applicants' results in Table 8A indicate that each of SEQ ID NO: 26, 27 and 28 (the last 20 amino acids of the human α-2a, -2b, and -2c adrenergic receptors, receptor) each bind to PDZ proteins of all four types (e.g., PSD-95, CASK, NOS and Mint 1). Because each of the three peptides have different sequences yet bind to each of a series of PDZ proteins known in the art to bind to different consensus sequences, the skilled artisan would question whether or not any of these interactions is biologically significant. Furthermore, even if the binding between one particular PDZ protein and one of the receptor sequences is eventually shown to occur *in vivo*, it would not indicate that all of the other interactions occur *in vivo* - the other interactions may

just be artifacts based on the PDZ sequence similarity (in same class of PDZ domain). Finally, even if a PDZ protein is eventually shown to bind to an α2 adrenergic receptor C-terminus *in vivo*, this would not indicate that said binding correlates with an activity of the receptor that can be modulated. Modulation of the binding could antagonize, agonize or have no effect on receptor activity. For example, many proteins are known to bind to the α2a adrenergic receptor C-terminus, but the function of these proteins, termed "accessory proteins" remains unclear even long after the effective filing date of the instant application (see Zezula et al, 2008. British Journal of Pharmacology. 153: S184-S190). The art does not recognize that a protein that binds to the C-terminus of an α2 adrenergic receptor is necessarily required for the agonist-induced activity of the protein.

Applicants point to MPEP 2107.01 as stating that "if an invention is only partially successful in achieving a useful result, a rejection of the claimed invention as a whole based on a lack of utility is not appropriate".

Applicants' arguments have been fully considered but are not found persuasive. The Examiner does not dispute Applicants' characterization of MPEP 2107.01. However, in the instant case the claimed invention is not even partially successful in achieving a useful result. In view of the teachings of the art (described above), what would be required for a partially successful result would be an indication that interaction between a specific α2 adrenergic receptor and a specific PDZ receptor interaction actually occurs in a cell and in such a manner that modulation of the binding alters the receptor activity.

Applicants further argue "that there are clear indications that the claimed *in vitro* methods will succeed in identifying binding interactions that are physiologically relevant *in vivo*. Applicants point to "analogous methods [used] to identify physiologically relevant interactions between other PL ligands such as HPV E6 and cellular PDZs" ... and point to Example 10 of US2004/022298, wherein inhibitors of E6-PDZ were shown to have "a therapeutic effect *ex vivo*" (pg 8).

Applicants' arguments have been fully considered but are not found persuasive. Eventual success in determining a specific and substantial utility does constitute an

immediate real-world specific and substantial utility. While a particular scientific result may eventually lead (after further experimentation) to an invention with a specific and substantial utility, this does not provide a specific and substantial utility for the initial discovery. The initial result must have an immediate, real-world specific and substantial use in and of itself and not just constitute basic research that is the starting point for further research. With respect to the E6-PDZ interaction, the instant specification provides a single mention of E6 as an oncogene that is a PDZ binding protein. As such, the E6-PDZ interaction does not appear to be encompassed by the instant claims and cannot provide a utility for the claimed invention. Furthermore, the utility of that interaction is dependent on the additional results disclosed that provide evidence that the interaction is physiological relevant in a manner that can be manipulated for a therapeutic effect.

Applicants further argue that "one embodiment of the claimed methods involves a yeast two-hybrid assay", which has "been accepted by those of skill in the art as reasonably correlating with physiologically relevant *in vivo* binding". Applicants point to Sprinzak et al (2003) as "concluding that 50% of the interactions identified by the yeast two-hybrid system are biologically relevant."

Applicants' arguments have been fully considered but are not found persuasive. While the claims encompass a method of detecting binding using a two-hybrid assay, Applicants' results showing binding between the particular α2 adrenergic receptors and particular PDZ proteins were not generated using such an assay. Instead, Applicants used an *in vitro* cell-free binding assay that is significantly different from a yeast two-hybrid assay. Furthermore, it is not clear from Sprinzak whether the yeast proteins examined in their meta-analysis were full-length proteins (which are more physiologically relevant) or small fragments such as used in the instant experiments (which are less physiologically relevant). Thus, the percentage of biologically relevant interactions found with yeast two-hybrid systems is not relevant to the biological relevance of the results found in the working example. Finally, as described above, even if a particular adrenergic receptor-PDZ protein interaction does occur in a cell, this

does not indicate whether or not modification of said binding will actual modify the activity of the receptor protein.

Applicants further argue that "A2AR antagonists have a well-established therapeutic use" and point to Erb et al, 2000 in support.

The Examiner does not dispute that A2AR antagonists have a well-established therapeutic use, or the teachings of Erb et al. However, in the instant application the claimed invention has not been shown to correlate with antagonism of the A2A receptor.

In section (B), Applicants argue that commercial antibodies are available to PDZ proteins that bind to the α2 adrenergic receptor, for example the first five proteins listed in Table 8A. Applicants argue that the existence of such antibodies shows a real-world, established utility for a method of detecting the five target proteins. Applicants argue that the claimed methods have "utility as research tools, since they can be used to detect or quantify a PDZ protein in a sample that is bound by an AAR peptide". Applicants provide the examples of tissue typing neuronal and endocrine by measuring NeDLG (a neuronal and endocrine-tissue specific protein), and diagnosis of prostate cancer by measuring AIPC (which is highly expressed in prostate cancer).

Applicants' arguments have been fully considered but are not found persuasive.

First, the specification as originally filed does not assert detection of a PDZ protein in a sample as a utility for the claimed method. There is no assertion of the claimed method in tissue typing or cancer diagnosis in the specification as originally filed. Therefore, such an assertion cannot provide utility for the claimed invention at the time of filing.

Second, an antibody can be made to any newly discovered protein sequence regardless of whether any utility is known for that protein. The existence of an antibody to a protein does not alone provide evidence of a utility for a method of detection of said protein using said antibody.

Third, each AAR peptide (A2AR, A2BR and A2C4) binds to numerous PDZ polypeptides, as shown in Table 8A. NeDLG may be neuronal and endocrine specific, but it is not the only PDZ protein found in such tissues. For example, the specification of PCT/US02/24655 (to which the instant application claims priority) teaches that "[t]he first

PDZ proteins were identified as functioning to concentrate receptors at neuronal synapses or tight junctions. In the nervous system, typical PDZ domain-containing proteins contain three PDZ domains, one SH3 domain and one guanylate kinase domain. Examples of intracellular PDZ domain-containing proteins include LIN-2, LIN-7 and LIN-10 at the pre-synapse, and PSD95 at the post-synapse" (¶ 3; PCT/US02/24655 has the same specification as national stage application 10/485788, which is published as US 20050282743). Furthermore, cells of other tissues express numerous PDZ proteins. Thus, measuring binding of AAR protein or peptide to an unknown biological tissue would not distinguish between different types of tissue or tissue because the AAR protein would bind to multiple PDZ proteins in each tissue.

In summary, it is maintained that the instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation to determine which, if any, of the many PDZ protein-binding partners actually interacts with an alpha adrenergic receptor in a manner such that modulation of the interaction will result in modification of the receptor activity.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation. This portion of the rejection was set forth at pg 5 of the 7/13/07 Office Action.

Applicants' arguments (6/16/08; pg 6-9) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response at pg 6-8, Applicants submit that as the claimed invention is supported by a specific and substantial asserted utility.

Applicants' arguments have been fully considered but are not found persuasive. For the reasons described above in the section "Claim Rejections – 35 USC § 101", the claimed invention is not supported by a specific and substantial asserted utility, and therefore it is maintained that one of skill would not know how to use the claimed invention without undue experimentation.

Even if the claimed invention was supported by a specific and substantial asserted utility or a well established utility, claims 1-4 would still be rejected under 35 U.S.C. 112, first paragraph. This portion of the rejection was set forth at pg 5-8 of the 7/13/07 Office Action.

Applicants' arguments (6/16/08; pg 9-10) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants submit that claim 1 has been amended to "recite a polypeptide "containing an alpha 2 adrenergic receptor C-terminal peptide sequence comprising the last 3 consecutive amino acids at the C-terminal end of SEQ ID NO: 26, SEQ ID NO: 27 or SEQ ID NO: 28" in order to more clearly specify that the polypeptide is in fact derived from the very C-terminal end of AARs" (pg 10).

Applicants' arguments have been fully considered but are not found persuasive. The specification does not teach any sequences other than SEQ ID NO: 26, 27 and 28 that can bind to PDZ proteins. The specification does not teach any smaller fragments of SEQ ID NO: 26, 27 and 28 can bind to PDZ. The recited sequences of SEQ ID NO: 26 (RIV), 27 (TAW) and 28 (FRQ) do not match any of the known consensus PDZ-binding sequences known in the art at the effective filing date of the instant application. See Bezprozvanny et al, 2001 (FEBS. 509: 457-462), who teaches that type I PDZ domains are specific for the consensus sequence S/T-X-Φ (where Φ is a hydrophobic amino acid); type II PDZ domains are specific for the consensus sequence Φ-X-Φ; that the PDZ protein nNOS is specific for the sequence G-E/D-X-V; and that the PDZ protein

Mint1-1 is specific for the sequence E/D-X-W-C/S (pg 457). Applicants' results in Table 8A indicate that each of SEQ ID NO: 26, 27 and 28 (the last 20 amino acids of the human α-2a, -2b, and -2c adrenergic receptors, receptor) each bind to PDZ proteins of all four types (e.g., PSD-95, CASK, NOS and Mint 1). Applicants appear to hypothesize that the last 3 residues of SEQ ID NO: 26, 27 or 28 (different in each case) must bind to each of these four different types of PDZ domains (each of which has a different consensus sequence), and are claiming a method using protein sequences as short as these three amino acids (include longer protein variants comprising the recited three amino acids). However, based on the teachings of Bezprozvanny, the skilled artisan would not predict that the three amino acids at the C-terminus of SEQ ID NO: 26 are necessarily those that bind each PDZ protein. The skilled artisan would need to engage in experimentation to determine whether or not peptides with less than all 20 amino acids of SEQ ID NO: 26 could bind to a PDZ protein of each type, and whether a representative number of variants of longer proteins comprising SEQ ID NO: 26, 27 and 28 could bind. Due to the large number of peptides to be tested (including fragments as small as 3 amino acids and from each of the three sequences of SEQ ID NO: 26, 27 and 28, and variants comprising said sequences), it is maintained that it would require undue experimentation to make and use the full scope of the claimed invention.

New rejections necessitated by Applicants' amendment

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the alpha 2 adrenergic receptor polypeptide" in lines 7-8. There is insufficient antecedent basis for this limitation in the claim. Specifically, claim 1 as amended defines "a polypeptide … comprising an alpha 2

adrenergic receptor C-terminal PL sequence comprising the last 3 consecutive amino acids at the C-terminal end of SEQ ID NO: 26, SEQ ID NO: 27 or SEQ ID NO: 28" as a "PL polypeptide" (line 3). This polypeptide is referred to as "the PL polypeptide" in the additional recitations of dependent claims 2-4. However, the concluding sentence of claim 1 refers to "the alpha 2 adrenergic receptor polypeptide". The antecedent basis of this recitation is unclear. If the antecedent basis is the PL polypeptide, this should be clearly indicated by referring to it as "the PL polypeptide" rather than "the alpha 2 adrenergic receptor polypeptide". If the antecedent basis differs from the PL polypeptide, this should be established in the claim.

The remaining claims are rejected for depending from an indefinite claim.

Conclusion

No claims are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Z. C. H./
Examiner, Art Unit 1646

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646